

AMENDMENT

This listing of claims will replace all prior versions, and listings, of claims in the present application.

1. (Currently amended) A recombinant herpes simplex virus incapable of expressing ~~only one~~ an active γ_1 34.5 gene ~~copy~~ product and comprising an expressible GM-CSF-encoding cytokine-encoding DNA.

2. (Currently amended) The recombinant herpes simplex virus of claim 1 wherein said virus lacks all or part of a said γ_1 34.5 gene ~~copy~~ genes.

3. (Canceled)

4. (Currently amended) The recombinant herpes simplex virus of claim 1 ~~3~~ wherein said virus comprises a γ_1 34.5 gene ~~genes~~ having a deletion of a portion of a coding sequence of said γ_1 34.5 gene ~~genes~~, said deletion comprising a Bst EII-StuI fragment of said γ_1 34.5 gene ~~genes~~.

5. (Currently amended) The recombinant herpes simplex virus of claim 1 wherein said virus comprises a γ_1 34.5 gene ~~genes~~ having a stop codon at a Bst EII site in said γ_1 34.5 gene ~~genes~~.

6. (Canceled)

7. (Currently amended) The recombinant herpes simplex virus of claim 1 wherein said expressible GM-CSF-encoding ~~cytokine-encoding~~ DNA is under the promoter-regulatory control of a herpes simplex virus gene promoter.

8. (Original) The recombinant herpes simplex virus of claim 7 wherein said herpes simplex virus gene promoter is an EGR-1 promoter.

9. (Currently amended) The recombinant herpes simplex virus of claim 1 wherein said GM-CSF-encoding ~~cytokine-encoding~~ DNA is under the promoter-regulatory control of a synthetic herpes simplex virus-derived promoter.

10. (Original) The recombinant herpes simplex virus of claim 9 wherein said synthetic herpes simplex virus-derived promoter comprises a herpes simplex virus α gene promoter fragment operatively linked 5' to a herpes simplex virus γ gene promoter fragment.

11. (Original) The recombinant herpes simplex virus of claim 10 wherein said α gene promoter fragment comprises promoter sequences upstream of the transcription initiation site of the α 4 gene and said γ gene promoter fragment comprises a transcription initiation site and the 5' transcribed non-coding sequence of the γ_1 U_L19 gene.

12. (Currently amended) The recombinant herpes simplex virus of claim 1 wherein a said γ_1 34.5 gene copy is genes are replaced by said expressible GM-CSF-encoding cytokine-encoding DNA.

13. (Currently amended) The recombinant herpes simplex virus of claim 1 wherein said virus comprises two or more copies of said GM-CSF-encoding DNA-encoding cytokine.

14. (Canceled)

15. (Currently amended) The recombinant herpes simplex virus type 1 of claim 1 ~~14~~ were said GM-CSF-encoding DNA ~~IL-4 encoding DNA~~ has replaced a said γ_1 34.5 gene copy genes.

16. (Currently amended) The recombinant virus of claim 1 ~~14~~ wherein said GM-CSF-encoding DNA ~~DNA encoding IL-4 DNA~~ is under the promoter regulatory control of an EGF-1 promoter.

17. (Currently amended) The recombinant virus of claim 1 ~~13~~ wherein said GM-CSF-encoding DNA ~~IL-4 encoding eDNA~~ further comprises a polyadenylation signal.

18. (Currently amended) The recombinant virus of claim 17 ~~14~~ wherein said polyadenylation signal is a hepatitis B virus-derived polyadenylation signal.

19. (Currently amended) A method for treating neoplastic disease ~~of the central nervous system~~, the method comprising administering to a target tumor, a

recombinant herpes simplex virus ~~incapable of~~ expressing ~~only one~~ an active $\gamma_134.5$ gene ~~copy product~~ and comprising an expressible GM-CSF-encoding ~~cytokine-encoding~~ DNA, wherein the expressed GM-CSF ~~cytokine~~ augments tumor cell killing.

20. (Currently amended) The method of claim 19 wherein said recombinant herpes simplex virus lacks all or part of a said $\gamma_134.5$ ~~gene-copy genes~~.

21. (Canceled)

22. (Currently amended) The method of claim 19 wherein said recombinant herpes simplex virus comprises a $\gamma_134.5$ ~~gene~~ genes having a stop codon at a Bst EII site in said $\gamma_134.5$ ~~gene~~-genes.

23. (Canceled)

24. (Currently amended) The method of claim 19 wherein said recombinant herpes simplex virus comprises a $\gamma_134.5$ ~~gene~~ genes lacking a portion of the coding sequence corresponding to a Bst EII/StuI restriction fragment of said $\gamma_134.5$ ~~gene~~ genes.

25. (Currently amended) The method of claim 19 wherein said expressible GM-CSF-encoding ~~cytokine-encoding~~ DNA is under the promoter-regulatory control of a herpes simplex virus gene promoter.

26. (Previously presented) The method of claim 25 wherein said herpes simplex virus promoter is an EGR-1 promoter.

27. (Currently amended) The method of claim 19 wherein said GM-CSF-encoding ~~cytokine-encoding~~ DNA is under the promoter regulatory control of a synthetic herpes simplex virus-derived promoter.

28. (Currently amended) The method of claim 27 wherein said synthetic herpes simplex virus-derived promoter comprises a herpes simplex virus α gene fragment operatively linked 5' to a herpes simplex virus γ gene promoter fragment.

29. (Currently amended) The method of claim 28 wherein said α gene promoter fragment comprises a promoter sequence ~~sequences~~ upstream of the transcription initiation site of said α gene promoter fragment comprising ~~comprises~~ the transcription initiation site and the 5' transcribed non-coding sequence of the γ_1 U_L19 gene.

30. (Currently amended) The method of claim 20 wherein said γ_1 34.5 ~~gene is~~ genes are replaced by said expressible GM-CSF-encoding ~~cytokine-encoding~~ DNA.

31. (Currently amended) A pharmaceutical composition comprising in a pharmaceutically acceptable carrier, diluent, or adjuvant, a recombinant herpes simplex virus incapable of expressing only one an active γ_1 34.5 gene copy product, said virus comprising an expressible GM-CSF-encoding ~~cytokine-encoding~~ DNA, wherein the expressed GM-CSF ~~cytokine~~ augments tumor cell killing.

32. (Canceled)

33. (Previously presented) The method of claim 19, wherein the target tumor is a tumor of the central nervous system.